REMARKS

Claims 1-28 and 53-55 are pending in the instant application. Claim 5 is allowed. Claims 1-4, 6-28 and 53-55 have been rejected. Claims 1 and 53 have been amended. Support for these amendments is provided in the specification, for example at page 10, lines 6 to 23. No new matter is added by this amendment and entry is respectfully requested.

I. Requirements under 37 C.F.R. 1.821 through 1.825

The Examiner suggests that the application fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825 for reasons set forth in the Notice to Comply. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants are providing herewith a substitute paper and disk copy of the sequence listing believed to comply with all requirements of the sequence listing rules. Replacement of the current Sequence Listing with this substitute paper and CRF copy is respectfully requested. Applicants are also providing herewith a Statement in accordance with 37 C.F.R. 1.821 that the paper and computer readable copies are the same and include no new matter.

II. Rejection of Claims 1-4, 6-24, 28 and 53-55 under 35 U.S.C. § 102(b)

Claims 1-4, 6-24, 28 and 53-55 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Wicks et al. (WO 94/27156). The Examiner suggests that Wicks et al. discloses the use of antibodies and detectable labels and markers to detect troponin I and troponin C in a complex in sandwich assays and that the phrase "myofilament protein modification product" in the instant claims encompasses any complex formation, covalent or non-covalent.

Applicants respectfully traverse this rejection.

The objective of Wicks et al. is to distinguish between cardiac and skeletal TnI. At page 5, Wicks et al. teach use of several amino acid sequences derived from cardiac TnI that are taught not to be present in skeletal TnI. As taught at page 5, lines 19-20 of Wicks et al., these peptides were selected solely for the purpose of distinguishing cardiac TnI from skeletal TnI. Thus, these peptides have no pathophysiological relevance. That is, the sequences detected by Wicks et al. do not occur *in vivo*, and hence their presence in a biological sample is not associated with muscle damage.

In contrast, in the present invention, the myofilament protein modification products evaluated for in a biological sample occur *in vivo* and are associated with muscle damage. This is clearly taught in the specification, for example at page 10, lines 6-23, and clearly distinguishes the present invention from the teachings of Wicks et al.

Further, the peptides used by Wicks et al. are generic and antibodies raised against such peptides cross-react with other peptides. Thus, the peptides and antibodies of Wicks et al. lack the specificity required to distinguish between intact and degraded/modified forms and/or cardiac and skeletal forms of proteins of interest and relative amounts thereof. Therefore the antibodies and peptides of Wicks et al. lack the specificity required to assess and diagnose skeletal and cardiac muscle damage as claimed in the instant invention.

In an earnest effort to advance the prosecution of this case and to clearly distinguish the present invention from the method and peptides of Wicks et al., Applicants have amended claim 1 and 53 in accordance with teachings at page 10, lines 6-23, to state that the presence of the myofilament protein modification product in the biological sample is associated with muscle damage.

Wicks et al. does not teach all the elements of the claims

as amended. Further, Wicks et al. does not provide an enabling disclosure with respect to assessing muscle damage as required to anticipate the invention as claimed. See MPEP § 2121. Thus, withdrawal of this rejection under 35 U.S.C. § 102(b) is respectfully requested.

III. Rejection of Claims 1-2, 8-21, 25-28, 53 and 55 under 35 U.S.C. § 102(b)

Claims 1-2, 8-21, 25-28, 53 and 55 have been rejected under 35 U.S.C. 102(b) as being anticipated by Takahashi et al. (WO 96/10078). The Examiner suggests that Takahashi et al. disclose the use of antibodies and detectable labels and markers to detect myosin light chain 1 in a complex in sandwich assays having immobilized solid phases for the purpose of assaying irreversible cardiac damage from biological samples such as blood. The Examiner suggests that the use of antibodies and processes of Takahashi et al. would detect not only MLC-1, but fragments of MLC-1 from the amino terminal of MLC-1 within the scope of the phrase "myofilament protein modification product" of the claims. Thus, the Examiner suggests that Takahashi et al. inherently meets all claim limitations, even if the intent is not to detect cardiac MLC-1 fragments per se.

Applicants respectfully traverse this rejection.

The peptide used by Takahashi et al. is a portion of MLC-1 selected by a computer for its immunogenicity (see page 14, lines 1-2 of Takahashi et al.). This peptide does not occur *in vivo* and is not a pathophysiological marker of muscle damage.

In contrast, as discussed in detail in Section II, *supra*, in the present invention, the myofilament protein modification products evaluated for in a biological sample occur *in vivo* and are associated with muscle damage. This is clearly taught in the specification, for example at page 10, lines 6-23, and clearly distinguishes the present invention from the teachings of Takahashi et al.

Further, the peptide used by Takahashi is generic and antibodies raised against this peptide cross-react with other peptides. See page 18, lines 5 to 8 and page 19, Table 2 of Takahashi et al. Thus, the antibodies of Takahashi et al. lack the specificity required to distinguish between intact and degraded/modified forms and/or cardiac and skeletal forms of proteins of interest and relative amounts thereof. Therefore, the antibodies and peptides of Takahashi et al. lack the specificity required to assess and diagnose skeletal and cardiac muscle damage as claimed in the instant invention.

In an earnest effort to advance the prosecution of this case and to clearly distinguish the present invention from the method and peptides of Takahashi et al., Applicants have amended claim 1 and 53 in accordance with teachings at page 10, lines 6-23, of the instant specification to state that the presence of the myofilament protein modification product in the biological sample is associated with muscle damage.

Since Takahashi et al. does not teach all the elements of the claims as amended nor provide an enabling disclosure for such a method as required under MPEP § 2121 to anticipate the invention as claimed, this reference cannot anticipate the invention as claimed. Withdrawal of this rejection under 35 U.S.C. § 102(b) is therefore respectfully requested.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record.

Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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